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(54) Title: METHODS FOR PREPARATION OF BIOPROSTHETIC TISSUE AND IMPLANTABLE DEVICES COMPRISING
SUCH BIOPROSTHETIC TISSUE

(57) Abstract: The present invention provides methods of inactivating and removing infectious agents from tissues of use in biopro-
sthetic devices. The methods include the removal and blockage of binding sites on the tissues for the infectious agents. Also provided
are methods for blocking a site on an infectious agent that binds to a site on the tissue. The invention also provides a method for
preventing or reducing the calcification of a bioprosthetic tissue. The method includes removing or blocking a phospholipid calcium
nucleation site from the tissue.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61L2/00 A61L2/18 A01N1/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 008 292 A (DINH TAN THANH ET AL) 28 December 1999 (1999-12-28) column 3, line 33 - line 43 column 2, line 29 example 1	1-20, 23-32
X	US 4 729 139 A (NASHEF AWS S) 8 March 1988 (1988-03-08) column 2, line 55 - line 62 column 7, line 33 - line 36	1-20, 23-32

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/46088

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet):

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-20, 23-32

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-20, 23-32

Method of ELIMINATING OR REDUCING INFECTION in a biological material, comprising removing a binding site so that AN INFECTIOUS AGENT is prevented or inhibited from binding to the biological material.

2. Claims: 21-22

Method of TREATING a biological material, comprising REMOVING A BINDING SITE so that AN UNWANTED PROTEIN is prevented or inhibited from binding to the biological material.

3. Claims: 33-39

Method of ELIMINATING OR REDUCING INFECTION in a bioprosthetic tissue, comprising BLOCKING A BINDING SITE so that AN INFECTIOUS AGENT is prevented or inhibited from binding to the binding site.

4. Claims: 40-49

Method of ELIMINATING OR REDUCING INFECTION in a bioprosthetic tissue, comprising BLOCKING AN INFECTIOUS AGENT so that this agent is prevented or inhibited from binding to the tissue.

5. Claims: 50-60

Method of ELIMINATING OR REDUCING CALCIFICATION in a biological material, comprising REMOVING A PHOSPHOLIPID CALCIUM NUCLEATION SITE so that CALCIUM is prevented or inhibited from the binding to the biological material.

INTERNATIONAL SEARCH REPORT

tion on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6008292	A	28-12-1999	AT 204767 T 15-09-2001
		AU 1466799 A	16-06-1999
		CA 2312376 A1	10-06-1999
		DE 69801517 D1	04-10-2001
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		DK 1035877 T3	03-12-2001
		EP 1035877 A1	20-09-2000
		ES 2163898 T3	01-02-2002
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		PT 1035877 T	28-12-2001
		WO 9927979 A1	10-06-1999

US 4729139	A	08-03-1988	NONE
